REMARKS

Reconsideration of the rejections set forth in the Office action mailed November 24, 2008 is respectfully requested. Claims 31-47 are pending in the application.

I. Amendments

Independent claim 31 has been amended to replace the phrase "improving the pharmacokinetics of a drug" with "inhibiting the metabolism of a drug". Support is found in the specification at, for example, page 3, line 6; page 17, line 34; page 18, lines 25-26; and page 36, line 4.

Independent claims 31 and 40 have been amended to recite that the morpholino antisense oligomer has "a base sequence exactly complementary to a target sequence in an RNA molecule which encodes the mammalian cytochrome p450 enzyme". Support is found in the original claims, which state that the antisense oligomer "hybridizes to" a target RNA molecule, and in the definition of "antisense" at page 5, line 32 to page 6, line 2: "The terms 'antisense oligonucleotide' and 'antisense oligomer' are used interchangeably and refer to an oligomer having a sequence of nucleotide bases and a subunit-to-subunit backbone that allows the antisense oligomer to *hybridize to a target sequence in an RNA*... The oligomer may have *exact sequence complementarity* to the target sequence or near complementarity."

Dependent claims 33, 34, 36 and 42-44 have been amended accordingly.

Independent claims 31 and 40 have also been amended, for clarity, to recite that the morpholino antisense oligomer has a backbone composed of morpholino subunit structures joined by phosphorodiamidate linkages. Support is found, for example, at page 7, line 8 of the specification.

Independent claim 40 has been amended to specify that the method is applied to a mammalian subject. Support is found, for example, at page 8, line 8 of the specification.

No new matter is added by any of the amendments.

II. Rejections under 35 U.S.C. §112, First Paragraph

A. Indefiniteness

Claims 31-47 were rejected under 35 U.S.C. §112, first paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant

regards as the invention. The Examiner's points are addressed in turn below.

The Examiner first asserted (paragraph 5) that the term "improving" in independent claim 31 was indefinite.

Applicant has addressed this objection by replacing the phrase "improving the pharmacokinetics of a drug" in claim 31 with "inhibiting the metabolism of a drug", as noted above.

The Examiner further asserted (paragraph 6) that independent claim 40 was indefinite in that its scope encompassed the administration of "any generic morpholino antisense oligomer targeting a cytochrome p450 enzyme" (page 3 of Office Action).

Applicant has addressed this objection by amending independent claim 40 to recite that the morpholino antisense oligomer has a "base sequence exactly complementary to a target sequence in an RNA molecule which encodes **the** mammalian cytochrome p450 enzyme", thus referring to the specific p450 enzymes recited in the preamble of the claim.

B. Written Description

Claims 31-35, 39-43 and 47 stand rejected and claims 36-38 and 44-46 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner made this rejection in view of the fact that the definition of "hybridizes to" in the specification encompasses oligomers having only "near complementarity" to the target sequence (page 4 of Office Action; paragraph 10).

Applicant has addressed this objection by amending independent claims 31 and 40 to recite that the morpholino antisense oligomer has "a base sequence **exactly complementary to** a target sequence in an RNA molecule", as noted above.

The Examiner also asserted that the scope of claim 40 encompassed "antisense oligomers targeting all other forms of mammalian cytochrome p450 enzymes", and that the claimed method was not limited to a mammalian subject (paragraph 11).

Applicant has addressed this objection by amending independent claim 40 to recite that the morpholino antisense oligomer has a "base sequence exactly complementary to a target sequence in an RNA molecule which encodes **the** mammalian cytochrome p450 enzyme", thus referring to

the specific p450 enzymes recited in the preamble of the claim, as noted above. Independent claim 40 has also been amended to specify that the method is applied to a mammalian subject.

The Examiner further asserted (page 5; paragraph 12) that the term "improving" in independent claim 31 rendered the scope of the claims unclear.

Applicant has addressed this objection by replacing the phrase "improving the pharmacokinetics of a drug" in claim 31 with "inhibiting the metabolism of a drug", as noted above.

The Examiner also stated that "the instant claims do not define the nucleotide structure of the target RNA molecule[s] which encode the target enzymes" (page 6 of Office Action). However, as disclosed in the specification, the nucleotide sequences of the genes encoding the p450 enzymes listed in the independent claims, and many others, were publicly available at the time of the filing of the application:

> "Sequences for numerous p450 genes of various species are known and available to those of skill in the art through public databases such as GenBank and review articles such as…" (page 12, lines 30-31); "Target sequences, including genomic sequences, pre-mRNA, mRNA, and/or cDNA sequences, from genes selected according to the considerations outlined in the previous sections, may be obtained from the GenBank sequence database or from other published sources readily available to those of skill in the art. As noted above, sequences for numerous rat and human p450 genes are known and available to those of skill in the art through sources such as GenBank and review articles such as Gonzales 1989, Black *et al.* 1987, and Nelson *et al.* 1993, cited above. For example, Nelson *et al.* lists all database accession numbers for p450 genes that were available in the GenBank/EMBL, SwissProt, and NBRF-PIR databases as of December 1992. Accession numbers for human p450 sequences are included from the following families: CYP-1A1, 1A2, 2A6, 2A7, 2B6, 2B7P, 2C8, 2C9, 2C10, 2C17, 2C18, 2C19, 2D6, 2D7P, 2D8P, 2E1, 2F1, 3A3, 3A4, 3A5, 3A7, 4A9, 4A11, 4B1, 4F2, 4F3, 5, 7, 11A1, 11B1, 17, 19, 21A1P, 21A2, and 27. Since the publication of the 1993 article, other human sequences, such as those for CYP-1B1 and CYP-2B1, have also been made available in GenBank." (page 18, line 31 to page 19, line 9)

In view of this publicly available sequence information and guidance in the specification, one skilled in the art would have been able to determine the sequences of antisense oligomers whose use is encompassed by the claimed methods.

In addition, as noted above, the independent claims now recite that the morpholino antisense oligomer has "a base sequence **exactly complementary to** a target sequence in an RNA molecule", obviating the alleged necessity of determining "which oligomers having 'near complementarity' to the target possess the function recited in the instant claims" (page 6 of Office Action).

C. Enablement

Claims 31-47 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and use the invention without undue experimentation.

The Examiner found that the specification was enabling "for a method of inhibiting cytochrome p450 …comprising the administration of morpholino antisense oligomers targeting RNA molecules encoding CYP1A1, CYP1A2, CYP2A6, CYP2B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4, wherein said antisense oligomers are fully complementary to the target RNA encoding these enzymes" and for "inhibiting the metabolism of drugs that are metabolized by CYP1A1, CYP1A2, CYP2A6, CYP2B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4, comprising the co-administration of morpholino antisense targeting these enzymes" (page 7 of Office Action).

Applicant submits that the claims now pending are in accordance with this scope of enablement.

In view of the foregoing, the applicant respectfully requests that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

III. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted,

/ LeeAnn Gorthey /

Date: February 24, 2009

LeeAnn Gorthey
Registration No. 37,337

Correspondence Address:
PAYOR NUMBER 79975
PHONE: (650) 590-0700